Acquired Hemochromatosis with Pronounced Pigment Deposition of the Upper Eyelids

ANNA H. CHACON, MD; BRIAN MORRISON, MD; SHASA HU, MD
Department of Dermatology & Cutaneous Surgery, University of Miami Miller School of Medicine, Miami, Florida

ABSTRACT

Hemochromatosis may be classified into two groups: primary (hereditary) or secondary (acquired). The acquired type most commonly occurs after massive intake of iron supplements or blood transfusions and is also known as transfusional iron overload. In the past, hemochromatosis was usually recognized at an advanced stage by the classic triad of hyperpigmentation, diabetes mellitus ("bronze diabetes"), and hepatic cirrhosis. Cutaneous hyperpigmentation is present in 70 percent of patients due to two different mechanisms: (1) hemosiderin deposition resulting in diffuse, slate-gray darkening and (2) increased production of melanin in the epidermis. A 47-year-old woman who receives regular transfusions due to low iron and chronic, unresolving anemia and who subsequently developed pronounced hyperpigmentation of the upper eyelids is described. The presentation, diagnosis, pathogenesis, and treatment options of hyperpigmentation due to secondary hemochromatosis are discussed. (*J Clin Aesthet Dermatol.* 2013;6(10):44–46.)

Acquired (secondary) hemochromatosis is a remarkable condition caused by chronic iron overload commonly due to frequent transfusions of red blood cells or excessive intake of iron. The characteristic cutaneous manifestation is a gray-to-brown mucocutaneous hyperpigmentation particularly pronounced in the sun-exposed areas of the face, dorsal hands, forearms, and inguinal area.[1] In up to 20 percent of patients with hereditary hemochromatosis, the mucous membranes are pigmented.[2,3] Other associated findings include alopecia, pruritus, localized icthyosis, and koilonychia.[4,5] A biopsy of affected hyperpigmented skin changes typically shows hemosiderin deposition in the dermis; however, the visible pigmentation manifests as increased melanin in the basal layer of the epidermis.[6] The authors report the first case of a 47-year-old woman with acquired hemochromatosis in which hyperpigmentation of the upper eyelids was particularly enhanced.

CASE REPORT

A 47-year-old disabled woman presented for a routine skin exam complaining of hyperpigmented areas on the face. The hyperpigmented macules and patches have been present for approximately 20 years since she was diagnosed with her celiac disease and began receiving transfusions regularly due to low iron and chronic, unresolving anemia. The hyperpigmented areas are mostly located on the extensor surfaces of the extremities, the upper chest and back, and several aspects of the face including the temples, upper eyelids, and perioral area. Associated symptoms include: persistent poor appetite and nausea, which she attributes to iron tablets. Other symptoms include chronic abdominal pain, frequent nocturia, dysuria, chronic fatigue, muscle weakness, numbness, tingling, frequent headaches, and easy bruising.

Past dermatological history is significant for several blistering sunburns, increased bruising, and poor healing over the past few years. Past medical history is significant for various autoimmune disorders, such as celiac disease, Sjogren's syndrome, antiphospholipid antibody syndrome, Meniere's disease, Graves' disease, and hypoparathyroidism. The patient also reports a history of depression, inflammatory bowel disease, and anemia of chronic disease requiring frequent transfusions of red blood cells.

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ADDRESS CORRESPONDENCE TO: Anna H. Chacon, MD; E-mail: annachaconmd@gmail.com

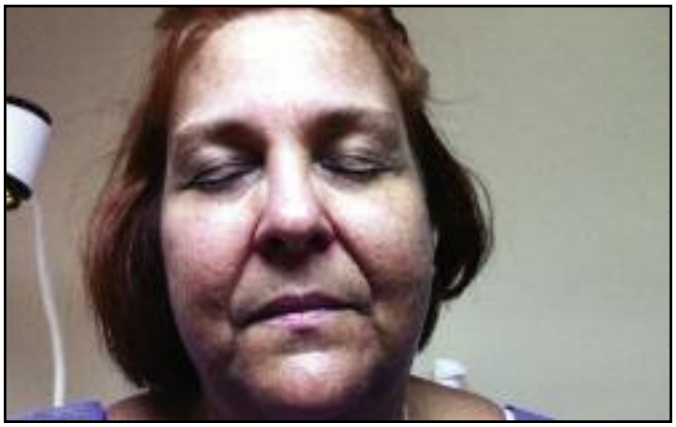

Figure 1. Frontal view of the face demonstrating a slate-gray hyperpigmentation pronounced on the upper eyelids and the perioral area

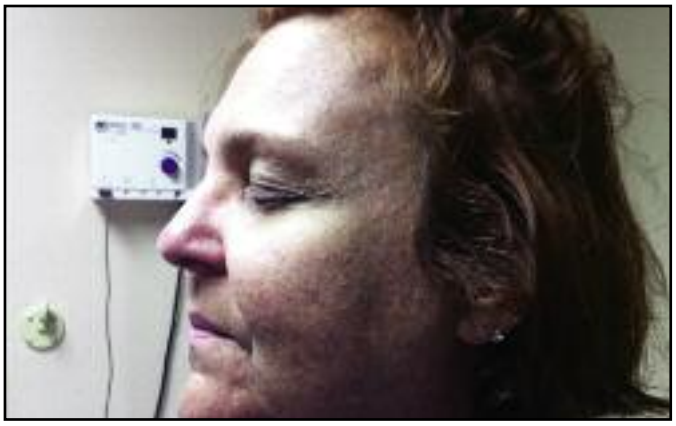

Figure 2. Profile view of the face demonstrating a slate-gray hyperpigmentation pronounced on the upper eyelids and the temples

Medications include ferrous sulfate 65mg orally twice daily; hydroxychloroquine 200 mg orally twice daily; aspirin; and other multivitamins, such as folic acid, vitamin A, biotin, calcium, cyanocobalamin, and vitamin D in recommended daily dosages. Other medications include pregabalin, diclofenac gel, duloxetine, armodafinil, esomeprazole, pancrelipase, tizanidine, liothyronine, darifenacin, oxycodone, levothyroxine, meclizine, and topiramate. Family history is remarkable for rheumatoid arthritis, gout, hypertension, renal disease, and coronary artery disease.

On physical exam, the authors observed flat, slate-gray hyperpigmented macules on the temples, upper and lower lip, and upper eyelids that were nontender to palpation (Figures 1 and 2). On further questioning, the patient denied using sunscreen regularly and acknowledges frequent sun exposure since she moved to Florida during grade school. The classical appearance of the macules, together with the history of frequent, chronic transfusions of red blood cells, suggested a diagnosis of hemosiderin hyperpigmentation due to acquired hemochromatosis. The patient was advised to use sunscreen regularly to avoid hyperpigmentation of sun-exposed areas.

DISCUSSION

Hyperpigmentation due to hemosiderin deposition also occurs in instances of hemorrhagic disease, chronic venous insufficiency, and purpura.[7] Sometimes a biopsy may be necessary to distinguish melanin versus hemosiderin-induced pigmentation.[8] While 30 percent of affected males and 10 percent of affected women with hereditary hemochromatosis have skin changes, the percentage of individuals with acquired hemochromatosis is similar given the fact that women lose iron during menstruation.[9,10]

Some medications, such as hydroxychloroquine, which this patient was taking for many years, deposit in the skin and complex with both iron and melanin, producing deposits with a unique, bluish gray color.[11] Additionally, the patient has been on numerous medications that may confound the true underlying etiology of her hyperpigmentation, including hydroxychloroquine, which may result in a mottled, reticulated, macular, gray pigmentation after several years of use.[12] Furthermore, the patient refuses to discontinue use of hydroxychloroquine, since she feels this medication helps control various associated symptoms related to her autoimmune disorders, such as inflammatory arthritis.

Another interesting feature in this case is the striking presentation of metallic gray hyperpigmentation on the upper eyelids. While it is well known that there is accentuation of sun-exposed and traumatized skin in hemochromatosis, the upper eyelids are not a commonly sun-exposed or traumatized area. Although buccal and conjunctival pigmentation, including recurrent sub-conjunctival hemorrhages, can be rare presenting signs of hemochromatosis, hyperpigmentation of the eyelids has never been reported as an associated ocular or cutaneous manifestation.[13] With early detection of associated hyperpigmentation of the eyelids in acquired hemochromatosis, dermatologists can make a reasonable judgment of possible causes based on the patient's history, leading to a significant impact on the quality of life and life expectancy of these patients.

Mortality in chronically transfused patients with thalassemia and sickle cell anemia is three times that of the general population in the United States and the most common cause of mortality is cardiomyopathy.[14] Although histological siderosis and clinical skin pigmentation may decrease if the patient chooses to undergo phlebotomies, she would prefer not to undergo this route due to her multiple medical problems and chronic anemia.[4] Monitoring for systemic symptoms, including hepatomegaly, elevated liver function tests, diabetes mellitus, impotence, amenorrhea, arthropathy, heart failure, and arrhythmias was recommended.[15] The patient was encouraged to avoid vitamin C supplementation, which increases iron availability and can worsen the disease by accelerating organ damage.[16]

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